

APPENDIX A: Bibliographic Databases Searched and Ovid Medline® Search Strategy (1946 to Jan 31, 2020)

Bibliographic Databases Searched (Inception to Jan 31, 2020)

The following databases were searched from inception to April 2018: Medline, Epub Ahead of Print and In-Process & Other Non-Indexed Citations, Embase Classic + Embase, Cochrane Central Register of Controlled Trials, Cochrane Database of Systematic Reviews, PsycINFO. The previous databases were all searched using the OvidSP platform. We also searched Web of Science from Clarivate Analytics and CINAHL from EBSCOhost.

Ovid Medline® Search Strategy (1946 to Jan 31, 2020)

#	Searches	Results	Type
1	Palliative Medicine/	310	Advanced
2	Palliative Care/	52691	Advanced
3	Hospice Care/	6324	Advanced
4	"Hospice and Palliative Care Nursing"/	740	Advanced
5	Terminal Care/	27484	Advanced
6	Terminally Ill/	6417	Advanced
7	exp Advance Care Planning/	9052	Advanced
8	exp Life Support Care/	8748	Advanced
9	palliat*.mp,kw.	83773	Advanced
10	hospice*.mp,kw.	14984	Advanced
11	advanced.mp,kw.	346600	Advanced
12	(advance* adj3 plan*).mp,kw.	5677	Advanced
13	(terminal* adj3 patient?).mp,kw.	7634	Advanced
14	(terminal* adj3 inpatient?).mp,kw.	44	Advanced
15	(terminal* adj3 outpatient?).mp,kw.	10	Advanced
16	(terminal* adj3 cancer?).mp,kw.	2613	Advanced
17	(terminal* adj3 care?).mp,kw.	28513	Advanced

18	(terminal* adj3 ill*).mp,kw.	11629	Advanced
19	(terminal* adj3 sick*).mp,kw.	35	Advanced
20	(terminal* adj3 disease?).mp,kw.	1838	Advanced
21	(terminal* adj3 stage?).mp,kw.	3540	Advanced
22	(terminal* adj3 failure?).mp,kw.	1754	Advanced
23	(terminal* adj phase?).mp,kw.	2026	Advanced
24	(terminal* adj mode?).mp,kw.	26	Advanced
25	(life adj3 threat*).mp,kw.	71982	Advanced
26	(life adj3 support*).mp,kw.	21456	Advanced
27	(support* adj3 care?).mp,kw.	35896	Advanced
28	(end adj3 life).mp,kw.	20304	Advanced
29	end-stage?.mp,kw.	59286	Advanced
30	palliat*.jw.	16332	Advanced
31	or/1-30	625782	Advanced
32	exp Analgesics, Opioid/	113791	Advanced
33	exp Opiate Alkaloids/	85189	Advanced
34	Methadone/	12138	Advanced
35	exp Naloxone/	25094	Advanced
36	Buprenorphine, Naloxone Drug Combination/	277	Advanced
37	exp Opioid-Related Disorders/	25634	Advanced
38	opiod?.mp,kw.	103621	Advanced
39	opiate?.mp,kw.	25636	Advanced
40	opium?.mp,kw.	2946	Advanced

41	algopan*.mp,kw.	1	Advanced
42	biopon*.mp,kw.	12	Advanced
43	cofapon*.mp,kw.	0	Advanced
44	laudan?n.mp,kw.	0	Advanced
45	laudopan*.mp,kw.	0	Advanced
46	nepenthe*.mp,kw.	185	Advanced
47	omnophon*.mp,kw.	33	Advanced
48	opial?.mp,kw.	3	Advanced
49	ophon?.mp,kw.	629	Advanced
50	oposal?.mp,kw.	1	Advanced
51	pantophon*.mp,kw.	9	Advanced
52	papaveretum*.mp,kw.	136	Advanced
53	pavon?.mp,kw.	86	Advanced
54	tetraphon?.mp,kw.	2	Advanced
55	53663-61-9.rn.	1	Advanced
56	8002-76-4.rn.	0	Advanced
57	8008-60-4.rn.	1990	Advanced
58	methadon*.mp,kw.	15209	Advanced
59	adanon*.mp,kw.	0	Advanced
60	algidon*.mp,kw.	0	Advanced
61	algolysin*.mp,kw.	2	Advanced
62	algoxale*.mp,kw.	0	Advanced
63	althose*.mp,kw.	0	Advanced

64	amidon*.mp,kw.	131	Advanced
65	amidosan*.mp,kw.	0	Advanced
66	(an 148 or an148).mp,kw.	9	Advanced
67	anadon*.mp,kw.	20	Advanced
68	biodone*.mp,kw.	0	Advanced
69	butalgin*.mp,kw.	3	Advanced
70	deamin.mp,kw.	1	Advanced
71	depidol*.mp,kw.	4	Advanced
72	diaminon.mp,kw.	1	Advanced
73	dianone*.mp,kw.	0	Advanced
74	dolafin*.mp,kw.	0	Advanced
75	dolamid*.mp,kw.	1	Advanced
76	dolesone*.mp,kw.	0	Advanced
77	dolmed*.mp,kw.	8	Advanced
78	dolophine*.mp,kw.	27	Advanced
79	dorex*.mp,kw.	1	Advanced
80	eptadone*.mp,kw.	2	Advanced
81	fenadon*.mp,kw.	10	Advanced
82	gobbidona*.mp,kw.	0	Advanced
83	heptadon*.mp,kw.	5	Advanced
84	heptanon.mp,kw.	5	Advanced
85	(hoe 10820 or hoe10820).mp,kw.	0	Advanced
86	ketalgin*.mp,kw.	0	Advanced

87	l-polamidon*.mp,kw.	6	Advanced
88	mecodin*.mp,kw.	3	Advanced
89	mepecton*.mp,kw.	0	Advanced
90	mephenon*.mp,kw.	0	Advanced
91	metadol*.mp,kw.	7	Advanced
92	metadon*.mp,kw.	247	Advanced
93	metasedin*.mp,kw.	0	Advanced
94	methaddict*.mp,kw.	1	Advanced
95	methados*.mp,kw.	5	Advanced
96	methaforte*.mp,kw.	0	Advanced
97	methex.mp,kw.	0	Advanced
98	miadone*.mp,kw.	4	Advanced
99	moheptan*.mp,kw.	0	Advanced
100	pallidone*.mp,kw.	2	Advanced
101	phenadon*.mp,kw.	9	Advanced
102	phymet.mp,kw.	0	Advanced
103	physepton*.mp,kw.	4	Advanced
104	physeptone*.mp,kw.	4	Advanced
105	polamidon*.mp,kw.	62	Advanced
106	polamiv?t*.mp,kw.	8	Advanced
107	sinalgin*.mp,kw.	0	Advanced
108	symoron*.mp,kw.	1	Advanced
109	westadone*.mp,kw.	0	Advanced

110	1095-90-5.rn.	0	Advanced
111	125-56-4.rn.	0	Advanced
112	23142-53-2.rn.	0	Advanced
113	297-88-1.rn.	0	Advanced
114	76-99-3.rn.	0	Advanced
115	naloxon*.mp,kw.	25907	Advanced
116	nalaxon*.mp,kw.	12	Advanced
117	antioplaz*.mp,kw.	0	Advanced
118	(en 1530 or en1530).mp,kw.	0	Advanced
119	(en 15304 or en15304).mp,kw.	0	Advanced
120	evzio.mp,kw.	9	Advanced
121	maloxone*.mp,kw.	4	Advanced
122	mapin.mp,kw.	2	Advanced
123	(mrz 2593 or mrz2593 or mrz 2593br).mp,kw.	2	Advanced
124	nalone*.mp,kw.	3	Advanced
125	narcan*.mp,kw.	91	Advanced
126	narcon*.mp,kw.	23	Advanced
127	narvcam*.mp,kw.	0	Advanced
128	naxone*.mp,kw.	0	Advanced
129	zynox.mp,kw.	0	Advanced
130	357-08-4; 465-65-6.rn.	0	Advanced
131	bunavail*.mp,kw.	7	Advanced
132	suboxone*.mp,kw.	119	Advanced

133	zubsolv*.mp,kw.	13	Advanced
134	or/32-133	185837	Advanced
135	31 and 134	7180	Advanced
136	exp animals/ not (exp animals/ and exp humans/)	4669549	Advanced
137	135 not 136	6978	Advanced
138	limit 137 to "all child (0 to 18 years)"	717	Advanced
139	limit 137 to "all adult (19 plus years)"	3437	Advanced
140	138 not 139	327	Advanced
141	137 not 140	6651	Advanced

Appendix B: Grey Literature Search Strategy

The following organizations' websites were searched for conference abstracts: Canadian Hospice Palliative Care Conference, American Academy of Hospice and Palliative Medicine (AAHPM), European Association for Palliative Care (EAPC), the American Society of Clinical Oncology (ASCO), the Multinational Association of Supportive Care in Cancer (MASCC), Palliative and Supportive Care in Oncology Symposium

TRIP (Clinical Search Engine), May 30, 2018

(palliat* OR hospice* OR advanced OR terminal* OR end of life) (opioid* OR opiate* OR opium* OR naloxone* OR suboxone*)

Open Grey (Multidisciplinary Open Access Repository), May 31, 2018

(palliat* OR hospice* OR advanced OR terminal* OR "end of life" OR "end stage") AND (opioid* OR opiate* OR opium* OR naloxone* OR suboxone*)

Google Custom Search: Canadian Government Documents May 31, 2018 (Maintained by Carleton University)

palliative | hospice | advanced | terminal | terminally | "end of life" | "end stage" opioid | opiate| methadone | naloxone | suboxone filetype:pdf

National Health and Medical research Council: Australian Government (NHMRC), May 31, 2018

(palliative or hospice or "end of life" or "end stage") and (opioid or methadone or naloxone or suboxone)

National Institute for Health and Care Excellence (NICE), May 31, 2018

((palliative care or hospice or "end of life" or "end stage" or advance or terminal) and (opioid or opiate or methadone or naloxone or suboxone))

Google, May 30, 2018

palliative | hospice | advanced | terminal | terminally | "end of life" | "end stage" opioid | opiate| methadone | naloxone | suboxone site:.int filetype:pdf

Google, May 30, 2018

palliative | hospice | advanced | terminal | terminally | "end of life" | "end stage" opioid | opiate | methadone | naloxone | suboxone filetype:pdf site:.org

Google May 30, 2018

palliative | hospice | advanced | terminal | terminally | "end of life" | "end stage" opioid | opiate | methadone | naloxone | suboxone site:.ca filetype:pdf

Google, May 30, 2018

palliative | hospice | advanced | terminal | terminally | "end of life" | "end stage" opioid | opiate | methadone | naloxone | suboxone site:.gov filetype:pdf

Google, May 30, 2018

palliative | hospice | advanced | terminal | terminally | "end of life" | "end stage" opioid | opiate | methadone | naloxone | suboxone site:.uk filetype:pdf

Google, May 30, 2018

palliative | hospice | advanced | terminal | terminally | "end of life" | "end stage" opioid | opiate | methadone | naloxone | suboxone filetype:pdf related:/association

Appendix C: Hierarchy of Importance

The developed reasons for exclusion and hierarchy of importance discussed were:

Most important reason

1. Unable to retrieve full text *
2. Duplicate*
3. Unable to translate *
4. 'wrong study design' (ex. opinion article, commentary)
5. 'wrong population' (ex. pediatrics, geriatrics)
6. 'wrong intervention' (ex. strategies to reduce opioid induced constipation)
7. 'wrong outcome' (ex. prescribing errors that result in overdose)
8. Others (New reasons that come up during screening that aren't captured by the above 6 reasons)

Least important reason

Appendix D: Information about development and validation of questionnaires used to assess for problematic opioid use in palliative care

Tool	Original development and validation studies						Subsequent validation studies			
	Studies	Reported construct measured	Administration	Populations	Number of items (score range)	Cut-off score	Studies	Reported constructs measured	Administration	Populations
CAGE	Mayfield (1974); ⁹⁸ Ewing (1984) ⁹⁹	Current alcoholism	Clinician interview	<ul style="list-style-type: none"> • Veteran psychiatric inpatients • Medical & surgical hospital patients • Alcoholic rehabilitation patients 	4 (0 - 4)	≥1 or 2	Bush (1987); ¹¹² Barry (1990); ¹¹³ Buchsbaum (1991); ¹¹⁴ Magruder-Habbib (1993); ¹¹⁵ Chan (1994); ¹¹⁶ Dyson (1998); ¹¹⁷ Saitz (1999); ¹¹⁸ Aertegeets (2000); ¹¹⁹ Teitelbaum (2000); ¹²⁰ Saremi (2001) ¹²¹	<ul style="list-style-type: none"> • Alcoholism (past year or lifetime) • Alcohol abuse (current or lifetime) • Alcohol dependence (current or lifetime) • Drinking disorder • Heavy drinking (past year or lifetime) 	<ul style="list-style-type: none"> • Clinician interview • Patient completed questionnaire (written or computer-assisted) 	<ul style="list-style-type: none"> • Inpatients (medical, orthopedic) • Outpatients (≥60 years old, American Indians, general medicine, Latinos, primary care, pregnant women, psychiatry, veterans)
CAGE-AID	Brown, 1995 ¹⁰⁰	Alcohol and drug ^A problems	Patient completed written questionnaire	Primary care outpatients	4 (0 - 4)	≥1 or 2	Dyson (1998); ¹¹⁷ Hinkin (2001); ¹²² Leonardson (2005); ¹²³ Couwenbergh (2009); ¹²⁴	<ul style="list-style-type: none"> • Drug problems (current or lifetime) • Alcohol and drug abusers • Substance abuse and dependence • Drug use and probable dependence • Substance use disorder 	Patient completed questionnaire completed at initial intake or 24 hours after admission	<ul style="list-style-type: none"> • Inpatients (adult psychiatric, medical or surgical; Dutch adolescents) • Northern Plains American Indians with type 2 diabetes • Parents and caretakers of Dutch adolescents admitted to mental health facilities

										<ul style="list-style-type: none"> • Korean patients with chronic pain taking strong opioid medications
ORT	Webster (2005) ²⁰	Likelihood of opioid related aberrant behaviors and opioid abuse 12 months after initial visit (screening)	Patient completed questionnaire	Patients prescribed opioids for chronic non-cancer pain	10 (0 - 26)	<ul style="list-style-type: none"> • Low risk 0-3 • Moderate risk 4-7 • High risk ≥8 	Moore (2009); ¹²⁵ Jones (2012); ¹²⁶ Witkin (2013) ¹⁰²	<ul style="list-style-type: none"> • Predict aberrant drug-related behavior among patients receiving opioids for pain management • Predict discharge from opioid treatment 	Patient completed written questionnaire on initial clinical visit	<ul style="list-style-type: none"> • New patients referred to pain clinic before opioid initiation • Pain centre
SOAPP	Butler (2004) ¹⁰⁴	Predict future medication misuse, aberrant behaviors and substance misuse	Patient completed written questionnaire	Chronic pain patients considered for long-term opioid therapy	24 (0 to 96)	≥7	Akbik (2006); ¹¹⁰ Moore (2009) ¹²⁵	<ul style="list-style-type: none"> • Risk for problems with long-term opioid medication • Risk of opioid abuse; • Risk for aberrant drug-related behavior 	Patient completed written questionnaire	<ul style="list-style-type: none"> • Patients considered for or taking opioids for chronic pain • New patients referred to pain clinic for treatment of pain with opioids
SOAPP SF	Butler (2004) ¹¹¹	Predict aberrant medication related behavior 6 months after initial testing	Patient completed written questionnaire	Chronic pain patients	5 (0 – 5)	≥4	Nil	Nil	Nil	Nil
SOAPP R	Butler (2008) ¹⁰⁵	Risk for aberrant opioid behavior	Patient completed written questionnaire	Chronic noncancer pain patients receiving long-	24 (0 to 96)	≥18	Butler (2009); ¹²⁷ Weiner (2016) ¹²⁸	<ul style="list-style-type: none"> • Risk for opioid abuse • Predict aberrant medication 	Patient completed written questionnaire	<ul style="list-style-type: none"> • Chronic noncancer pain management centre patients prescribed opioids

				term opioid therapy				related behavior within 6 months of initial testing		<ul style="list-style-type: none"> Emergency department patients being considered for discharge with prescription for opioid
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Note: CAGE: Cut Down, Annoyed, Guilty and Eye-Opener (alcoholism screen); CAGE-AID: CAGE-Adapted to Include Drugs (alcoholism and drug screen); ND: Not reported; ORT: Opioid Risk Tool; SOAPP: Screener and Opioid Assessment for Patients with Pain; SOAPP-R: SOAPP-Revised; SOAPP-SF: SOAPP-Short Form

A: Drugs defined as “street drugs and addictive medications that were beyond how they were prescribed”

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